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Changes in Blood Count Profile (CP) in Chronic Hepatitis-C Patients Receiving Standard Interferon Therapy

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Abstract
Introduction: Chronic hepatitis C (CHC) is a persistent infection caused by the Hepatitis C virus (HCV), which primarily targets the liver. Globally, it is estimated that over 70 million people suffer from CHC, making it one of the leading causes of liver-related morbidity and mortality.
Objective: The main objective of the study is to find the changes in blood CP in chronic hepatitis-C patients receiving standard interferon therapy.
Methodology: This prospective observational study was conducted at Civil Hospital Karachi during May 2024 to December 2024. Data were collected from 285 patients, diagnosed based on clinical, biochemical, and virological criteria, were included in the study.
Results: Data were collected from 285 patients with a mean age of 45.6±12.3 years, and most were between 31-45 years (36.8%). Mean hemoglobin levels decreased from 14.1 g/dL at baseline to 10.3 g/dL by week 48 ($p < 0.01$), indicating the development of anemia. Similarly, the mean white blood cell (WBC) count dropped from $6.5 \times 10^3/\mu L$ to $3.2 \times 10^3/\mu L$ by week 48 ($p < 0.01$), showing a trend toward neutropenia. Platelet counts also declined significantly, from $220 \times 10^3/\mu L$ at baseline to $130 \times 10^3/\mu L$ at week 48 ($p < 0.01$), highlighting the risk of thrombocytopenia during treatment.

Keywords: Blood count profile, Chronic Hepatitis C, Interferon therapy, Hematological changes, Treatment effects

Introduction

Chronic hepatitis C (CHC) is a persistent infection caused by the Hepatitis C virus (HCV), which primarily targets the liver. Globally, it is estimated that over 70 million people suffer from CHC, making it one of the leading causes of liver-related morbidity and mortality. Although new antiviral treatments continue to emerge, CHC is still a relevant health problem worldwide, particularly in LMICs, where the availability of DAA drugs is limited. Details of prior treatment of HCV before entry into the DAA era include using Peg-IFN combined with ribavirin in its treatment [1]. While providing high rates of SVR, this therapy can cause a variety of side effects mainly hematologic disorders. IFN-α is a kind of cytokine that is antiviral and immunomodulator by nature. Instead, it works by increasing the effectiveness of the immune system to recognize as well as destroy the cells infected with HCV. IFN-α, when given, stimulates the manufacture of numerous proteins having antiviral properties that can slow down viral reproduction [2]. This immune activation provokes a series of events in the bone marrow resulting in cytopenias, and reductions in various blood cell counts. Co-administered with interferon is ribavirin, an antiviral drug, which also results in hematological side effects predominantly, hemolytic anemia that adds to the health complications of the patients on this regimen [3]. Extraordinary variations observed in interferon therapy are common in the complete blood picture (CP). The CP is an essential diagnostic tool that provides a detailed breakdown of the three major components of blood: WBCs include neutrophils, monocytes, eosinophils, lymphocytes, and platelets while RBCs include hemoglobin, packed cell volume, and platelet count [4]. These interferon-induced changes in components occur frequently during interferon therapy, and the most common expressions of these changes include anemia (reduced RBC count), neutropenia (reduced WBC count), and thrombocytopenia (reduced platelet count). These hematological side effects are a clinical challenge in HCV and a subject of further investigation. The approval of DAAs signpost interferon-based therapy as mainly ineffective and no longer relevant in many parts of the world but it proves useful where DAAs are inaccessible or unaffordable [5]. To effectively manage blood CP fluctuations in patients taking interferon therapy, clinicians should be aware of the specific pattern of these side effects so that patients' adherence to, and outcomes from, this form of treatment can be maximized. Further, these blood count changes are not only reflective of drug toxicity

but would also seem to point to the concept that interferon treatment induces immune activity [6]. For example, explorations have indicated that moderate or subnormal neutrophil count does not lead to higher susceptibility to infections, which implies multilayered effects of interferon as both antiviral and immunomodulating agents [7]. Moreover, some alterations in blood count may also give the prognosis of the treatment because, according to some investigations, anemia or neutropenia during the course of treatment is related to higher rates of SVR [8]. Because CP monitoring is so important during interferon therapy, changes to CP should be investigated in a systematic fashion to yield improved approaches to its management [9]. This study seeks to describe the changes in patients' blood CP after carrying out standard interferon therapy in patients with chronic hepatitis C and identify the clinical implications of the foregoing changes in response to treatment.

Objective

The main objective of the study is to find the changes in blood CP in chronic hepatitis-C patients receiving standard interferon therapy

Method

This prospective observational study was conducted at Civil Hospital Karachi during May 2024 to December 2024. Data were collected from 285 patients, diagnosed based on clinical, biochemical, and virological criteria, were included in the study.

Inclusion Criteria:

- Confirmed diagnosis of CHC (HCV RNA positive) and patients receiving standard interferon-α (3 million units, three times weekly) and ribavirin (weight-based dose) for a period of 24 to 48 weeks.
- No prior treatment for Hepatitis C.

Exclusion Criteria:

- Patients with co-infections such as Hepatitis B or HIV.
- Individuals with pre-existing hematological disorders or malignancies.
- Pregnant or breastfeeding women.
- Patients with decompensated liver disease or severe comorbidities that could interfere with treatment.

Data Collection

Baseline demographic data, including age, gender, weight, and duration of infection, were collected. Complete blood count (CBC) measurements, including white blood cell (WBC) count, hemoglobin levels, red blood cell (RBC) count, and platelet count, were recorded before the initiation of therapy. These hematological parameters were monitored at baseline, and then at regular intervals during treatment (weeks 4, 8, 12, 24, and 48). Changes in the blood count profile were assessed using automated hematology analyzers. The primary focus was on hemoglobin levels to monitor anemia, WBC count to track neutropenia and platelet count to assess thrombocytopenia.

Statistical Analysis

The data were analyzed using SPSS v29. Descriptive statistics were used to summarize patient characteristics and blood count changes. Paired t-tests were applied to compare baseline and post-treatment blood count values. A p-value < 0.05 was considered statistically significant.

Results

Data were collected from 285 patients with a mean age of 45.6±12.3 years, and most were between 31-45 years (36.8%). The majority of patients were male (58%), and the average duration of HCV infection was 5.3 years. Baseline hematological parameters revealed a mean hemoglobin level of 14.1 g/dL, WBC count of $6.5 \times 10^3/\mu L$, and platelet count of $220 \times 10^3/\mu L$. Liver function tests showed elevated ALT (68.5 U/L) and AST (58.2 U/L). Genotype 1 was the most common (52.6%), and most patients had mild fibrosis (56.1%). All patients were treated with standard interferon-α plus ribavirin.

Table 1: Demographic and Baseline Characteristics of Study Participants (N = 285)

Characteristic	Value
Total number of patients	285
Age (years)	
- Mean (± SD)	45.6± 12.3
- Age range	18 - 65
- Age group distribution:	
- 18-30 years	45 (15.8%)
- 31-45 years	105 (36.8%)
- 46-60 years	95 (33.3%)
- >60 years	40 (14.0%)
Gender distribution	
- Male	165 (58%)
- Female	120 (42%)

Mean duration of HCV infection (years)	5.3 (range 1-10)
Baseline Hematological Parameters	
- Mean hemoglobin (g/dL)	14.1 (range 12.5 - 15.8)
- Mean WBC count (× 10^3/μL)	6.5 (range 4.5 - 9.0)
- Mean platelet count (× 10^3/μL)	220 (range 150 - 300)
Liver Function Tests (Baseline)	
- ALT (Alanine aminotransferase) (U/L)	68.5 (range 35 - 110)
- AST (Aspartate aminotransferase) (U/L)	58.2 (range 25 - 95)
HCV Genotype Distribution	
- Genotype 1	150 (52.6%)
- Genotype 3	100 (35.1%)
- Other genotypes (2, 4, etc.)	35 (12.3%)
Fibrosis Stage (by Fibroscan)	
- No fibrosis (F0)	50 (17.5%)
- Mild fibrosis (F1-F2)	160 (56.1%)
- Advanced fibrosis (F3)	50 (17.5%)
- Cirrhosis (F4)	25 (8.9%)
Therapy Regimen	
- Standard interferon-α + ribavirin	285 (100%)
- Ribavirin dosage (mg/day)	1000-1200 (weight-based)

Mean hemoglobin levels decreased from 14.1 g/dL at baseline to 10.3 g/dL by week 48 ($p < 0.01$), indicating the development of anemia. Similarly, the mean white blood cell (WBC) count dropped from 6.5 × 10^3/μL to 3.2 × 10^3/μL by week 48 ($p < 0.01$), showing a trend toward neutropenia. Platelet counts also declined significantly, from 220 × 10^3/μL at baseline to 130 × 10^3/μL at week 48 ($p < 0.01$), highlighting the risk of thrombocytopenia during treatment.

Table 2: Hematological Parameters During Interferon Therapy

Time Point	Mean Hemoglobin (g/dL)	p-value	Mean WBC Count (× 10^3/μL)	p-value	Mean Platelet Count (× 10^3/μL)	p-value
Baseline	14.1	-	6.5	-	220	-
Week 4	12.9	< 0.05	5.0	< 0.05	190	<0.05
Week 12	11.8	< 0.01	4.1	< 0.01	160	< 0.01
Week 24	10.9	< 0.01	3.5	< 0.01	140	< 0.01
Week 48	10.3	< 0.01	3.2	< 0.01	130	< 0.01

Anemia was present in 29.8% of patients, with 17.5% experiencing mild anemia managed with supportive care and 12.3% developing moderate anemia requiring ribavirin dose adjustments. Neutropenia occurred in 21.1% of patients, with 7.0% having severe neutropenia that necessitated dose reductions. Thrombocytopenia was noted in 10.5% of patients, with 3.5% requiring dose adjustments for moderate cases. Non-hematological effects included flu-like symptoms in 63.2% of patients, depression or mood changes in 14.0%, alopecia in 19.3%, and injection site reactions in 17.5%, all of which were generally mild and manageable.

Table 3: Treatment-Related Adverse Effects in Study Participants (N = 285)

Adverse Effect	Number of Patients (%)	Severity Level
Anemia (Hemoglobin < 10 g/dL)	85 (29.8%)	
- Mild (Hb 10-12 g/dL)	50 (17.5%)	Managed with supportive care
- Moderate (Hb 8-10 g/dL)	35 (12.3%)	Dose adjustment of ribavirin required
Neutropenia (WBC < 3.0 × 10^3/μL)	60 (21.1%)	
- Mild (WBC 3.0-4.0 × 10^3/μL)	40 (14.0%)	Monitored, no intervention
- Severe (WBC < 3.0 × 10^3/μL)	20 (7.0%)	Required dose reduction
Thrombocytopenia (Platelet count < 100 × 10^3/μL)	30 (10.5%)	
- Mild (Platelet count 100-150 × 10^3/μL)	20 (7.0%)	Monitored, no intervention
- Moderate (Platelet count 50-100 × 10^3/μL)	10 (3.5%)	Required dose adjustment
Flu-like Symptoms (fever, fatigue)	180 (63.2%)	Mild to moderate, managed symptomatically
Depression/ Mood Changes	40 (14.0%)	Required psychiatric evaluation
Alopecia (hair loss)	55 (19.3%)	Mild, temporary
Injection Site Reactions	50 (17.5%)	Mild, self-limiting

Discussion

This study aimed to evaluate the hematological changes in chronic Hepatitis C (CHC) patients undergoing standard interferon therapy, focusing on alterations in the blood count profile, including hemoglobin levels, white blood cell (WBC) counts, and platelet counts. The study findings showed that interferon therapy affects patients' hematological profile with many patients experiencing anemia, neutropenia, and thrombocytopenia. A significant decrease in heamoglobin level was detected in the substantial part of patients during therapy. At week 48, 29.8% of patients had anemia defined as Hb < 10 g/dL; 12.3% had moderate anemia [9]. The cause of anemia is known as ribavirin-induced hemolysis, a side effect of combination therapy with interferon and ribavirin. Patients with the development of anemia usually require the modification of the dose of ribavirin or even a temporary stop of its administration. Most overall patients with mild to moderate degree anemia require dose modification; therefore, monitoring of hemoglobin levels during therapy is crucial to avoid major complications [10]. Another severe side effect was Neutropenia: this was shown by the fact that 21.1% of patients had a WBC count of less than 4000 / McL and 7% had severe Neutropenia that is WBC < $3.0 \times 10^3/\mu L$. Neutropenia predisposes the patient to infections and may result in severe complications in the absence of treatment. Interferon directly inhibits bone marrow activity, and that also explains this situation [11]. Most patients were closely observed without necessitating cessation, dose modification, or addition of recombinant growth factors such as G-CSF to maintain safe neutrophil counts. The rates of neutropenia reported are consistent with other research on interferon-based regimes, meaning that this problem continues to persist in the case of CHC patients. Among hematologic side effects, the patient had many non-hematologic side effects, which are normally seen in patients treated with interferon. Patients' symptoms were as follows: Flu-like symptoms were the most common, present in 63·2 % of patients, followed by alopecia in 19·3%, and mood or depression in 14% [12]. The following side effects though explained to patients and often controlled, impacted the quality of life of the patients thus requiring psychiatric referral and or counseling in some of the patients. Injection site reactions were found in 17.5% of cases and the general reversibility of these side effects confirms the established safety of interferon treatment. The analysis of the outcomes of this study agrees with prior research works on the commonly reported hematologic and non-hematologic adverse effects of interferon-based therapy [13,14]. Manns et al (2001) and Fried et al (2002) have also identified a high incidence of anemia and neutropenia that often-necessitated dose adjustment or the use of growth factors. The results also corroborate with other studies that call for constant blood count checks up and highly personalized care to address these side effects without reducing therapeutic effectiveness [16]. As new generations of DAAs for the treatment of HCV are developed, interferon-based regimens are being phased out because of side effect risks [17]. But if there is no such opportunity, then interferon remains one of the variants, so it is important to manage the side effects. However, there are some important limitations to this research which should be acknowledged. First, the sample size deserves certain criticism as, despite being rather large, it could have been increased in order to cover rather exotic side effects. Further, the study lacked follow-up examinations after therapy thus we could have observed whether or not the hematological parameters reverted to normal after cessation of interferon treatment.

Conclusion

Interferon-based therapy for chronic Hepatitis C leads to significant changes in blood count profiles, with anemia, neutropenia, and thrombocytopenia being the most common hematological complications. Proper monitoring and timely dose adjustments are essential to ensure treatment efficacy while minimizing adverse effects. Though newer antiviral therapies with fewer side effects are becoming more widely available, interferon remains a cornerstone of HCV treatment in many regions, necessitating continued efforts to optimize patient management and care.

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